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2. (Twice Amended) An isolated nucleic acid comprising a nucleotide sequence encoding a protein selected from the group consisting of an hcAMP-GEFII protein having the amino acid sequence of SEQ ID NO: 18 a hormal variant of said hcAMP-GEFII protein, and a mutant of said hcAMP-GEFII protein, wherein said normal variant of said hcAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

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4. (Twice Amended) An isolated nucleic acid as in claim 2 wherein said nucleic acid encodes a normal variant of said hcAMP-GEFII protein, [and] wherein said nucleotide sequence comprises a sequence encoding a normal variant of said hcAMP-GEFII protein and capable of hybridizing under stringent hybridization conditions to a sequence complementary to a sequence encoding a protein comprising the human cAMP-GEFII amino acid sequence of SEQ ID NO: 18, and wherein said stringent hybridization conditions comprise a temperature between about 20°C and about 65°C and an ionic strength between about 5x SSC and about 0.1x SSC.

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9. (Twice Amended) An isolated nucleic acid comprising a nucleotide sequence encoding at least one functional domain of an hcAMP-GEF II protein having the amino acid sequence of SEQ ID NO. 18; a normal variant of said hcAMP-GEFII protein, or a mutant of said hcAMP-GEFII protein, wherein said normal variant of said hcAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

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11. (Twice Amended) An isolated nucleic acid comprising a nucleotide sequence encoding an antigenic determinant of an hcAMP-GEFII protein (SEQ ID NO: 18) and selected from the group consisting of a normal variant of said hcAMP-GEFII protein, and a mutant of said hcAMP-GEFII protein, wherein said normal variant of said hcAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *In vitro* assay.

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38. (Twice Amended) An isolated nucleic acid comprising a variant nucleotide sequence of a human cAMP-GEFII gene (SEQ ID NO: 17), said variant being selected from the group consisting of an allelic variant of said human cAMP-GEF II gene, and a heterospecific

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homologue of said human cAMP-GEFII gene, wherein said variant of said cAMP-GEFII gene encodes a protein that exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.

- 39. (Twice Amended) An isolated nucleic acid encoding a variant amino acid sequence of a human cAMP-GEFII protein (SEQ ID NO: 18), said variant being selected from the group consisting of an allelic variant of said human cAMP-GEF II protein, and a heterospecific homologue of said human cAMP-GEFII protein, and wherein said variant of said cAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.
- 42. (Amended) An isolated nucleic acid as in claim 41 wherein said expression vector may express said nucleotide sequence in mammalian cells in culture.
- 43. (Amended) An isolated nucleic acid as in claim 42 wherein said cells in culture are selected from the group consisting of fibroblast, liver, kidney, spleen, bone marrow, and neurological cells.

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- 45. (Twice Amended) An isolated nucleic acid as in claim 41 wherein said expression vector encodes at least a functional domain of a protein selected from the group consisting of an hcAMP-GEFII protein having the amino acid sequence of SEQ ID NO: 18, a normal variant of said hcAMP-GEFII, and a mutant of said hcAMP-GEFII, wherein said normal variant of said hcAMP-GEFII protein exhibits guanine nucleotide exchange factor activity in an *in vitro* assay.
- of any one of claims 41-49, or a descendant thereof, wherein said host cell is transformed *in vitro* with said expression vector.
- 51. (Amended) A host cell in culture as in claim 50 wherein said host cell is selected from the group consisting of bacterial cells and yeast cells.



- 52. (Amended) A host cell in culture as in claim 50 wherein said host cell is selected from the group consisting of fetal cells, embryonic stem cells, zygotes, gametes, and germ line cells.
- 53. (Amended) A host cell in culture as in claim 50 wherein said cell is selected from the group consisting of fibroblast, liver, kidney, spleen, bone marrow and neurological cells.
- 54. (Amended) A host cell in culture as in claim 50 wherein said cell is an invertebrate cell.

## **Basis for Amendments**

Claims 118 and 120 have been cancelled without prejudice and without the intention of abandoning the subject matter claimed therein. Indeed, Applicants may choose to pursue claims of the same scope, or narrower or broader scope, in the form of one or more related applications at a later date.

Claims 2, 9, 11, 38, 39 and 45 have been amended to recite that the protein corresponding to the claimed variant exhibits guanine nucleotide exchange factor activity in an *in vitro* assay. That amendment is supported in the specification at page 21, lines 10 and 11, and Example 2, starting on page 54.

Claim 4 has been amended to recite that the stringent hybridization conditions comprise a temperature of between about 20°C and about 65°C and an ionic strength between about 5x SSC and about 0.1x SSC. That amendment is supported in the specification at page 19, lines 10 and 11.

Claims 42 and 50-54 have been amended to recite a host cell in culture. That amendment is supported in the specification at page 5, line 14; page 30, lines 1-20; and original claim 103.

Attached is a marked-up copy of the amended claims, as well as a clean copy of the complete set of pending claims as amended. No new matter is introduced by those amendments.